REMARKS

References Cited on the PTO-1449 in Paper No. 11

In the 06/06/2003 Office Action, the Examiner stated that the references listed on the PTO-1449 in paper No. 11 were not present in the file and that if the Applicant submitted another set of the same references, the Examiner would consider them as though they were submitted with the IDS in paper No. 11. Applicant would like to make clear that the references were submitted with the original paper No. 11. However, as requested by the Examiner, Applicant is resubmitting a copy of the original IDS, PTO-1449 and the cited references and would appreciate if the Examiner will consider those references as though they were submitted with the original paper No. 11.

Observations on Examiner's Conclusions Regarding Entitlement to Priority

Applicant notes that the Examiner has made certain observations regarding the support for the present claims in one or more earlier-filed applications to which Applicant has claimed priority. Those observations led the Examiner to assert that the present claims are not entitled to a filing date prior to 12/07/01, the filing date of the instant application. *See* 06/06/03 Office Action at page 2. Applicant disagrees with the Examiner's assertion regarding the effective filing date of the present claims, and expressly reserves the right to fully dispute such assertion at a later time, if necessary.

In particular, Application maintains that the pending claims are entitled to at least the filing date of 8/24/00, the international filing date of priority document PCT/US00/23328 ("the '328 application"). Contrary to the Examiner's assertions that the Applicant's "provide no guidance or working examples to teach how to use the claimed invention," the '328 application does provide guidance to one skilled in the art that supports several substantial and specific utilities recited for the claimed polypeptides in the specification of the '328 and present applications. For example, the '328 application discloses that the claimed polypeptides are differentially expressed in diseased tissue as compared to a normal tissue of the same type. *See* p. 62, lines 34-37. Example 18 (p. 93 of the '328 application) shows that the polynucleotide encoding SEQ ID NO:2 is differentially expressed in normal esophagus versus esophageal tumor

tissue and rectum tumor tissue relative to normal rectum tissue. The above-cited evidence shows that the polypeptides of the current invention are useful diagnostically for the determination of the presence or absence of at least esophageal and rectal tumors in a subject suspected of possessing such tumors, as well as being a useful target for the treatment of such tumors. As such, the Applicant has demonstrated at least one specific, substantial and credible utility for the claimed inventions of the present application, and the claimed invention is entitled pursuant to 35 U.S.C. §120 to at least the filing date of the '328 application (i.e., at least 8/24/00).

Applicant specifically reserves the right to further address the basis of its entitlement to priority under 35 U.S.C. §120 to other applications not addressed in the preceding paragraph.

Objection to claims 33-40 under 37 C.F.R. § 1.821(d) for identifying a nucleotide sequence by a figure with SEQ ID NO: in parenthesis.

In view of the amendments made to claims 33-40, Applicant requests that the objection be removed.

Rejection of claims 33-43 for double patenting under 35 U.S.C. §101 and 37 C.F.R. § 1.178(b)

The Examiner maintains that the claims of this application conflict with the claims of Application No. 10/063,527 ("'527 application"). Accordingly, the Examiner requires that one set of conflicting claims be cancelled or that a clear line of demarcation be maintained between this and the '527 application.

Applicant is submitting concurrently with the present response an express abandonment for the '527 application. A copy of the express abandonment is attached for the examiner's convenience. On this basis, Applicant submits that the rejection is obviated, and the rejection should be withdrawn.

Rejection of claims 33-37 under 35 U.S.C. § 112, 1st paragraph, enablement

The Examiner maintains that the claims "read on any or all variants meeting the sequence limitation, and encoding polypeptides either with or without a functional activity." As such, the

Examiner maintains that the claims encompass "an unreasonable number of nucleic acids encoding inoperative polypeptides." Upon this basis, the Examiner maintains that a person of ordinary skill would have to engage in "undue experimentation to make and/or use the claimed invention in its full scope."

Applicants submit that the present claims are fully enabled by the present disclosure. The specification teaches one skilled in the art how to determine sequence identity (e.g., p. 17, line 16 to p. 19, line 6 and Tables 2 and 3 of the '328 application) and how to make polypeptides that vary in sequence identity but that will still exhibit biological activity of interest (see, e.g., p. 48, line 18 – p. 51, line 9 of the '328 application). Even assuming *arguendo* that some polypeptides encoded by sequences that fall within the scope of the claims may not exhibit the identical biological activity of the full sequence described therein, this is not a proper basis for rejecting the claims as being non-enabled. The Examiner has not, for example, provided evidence that would support the view that there are inoperative species within the claim scope or the nature of their "inoperability." The Examiner also has not established why a skilled artisan, equipped with the teachings of the present disclosure, would have any difficulty selecting particular sequences falling within the scope of the claims that retain the biological activity of interest. As *In re Wands,* 858 F.2d 731; 8 USPQ2d 1400 (Fed. Cir. 1988) itself emphasizes,

> Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. "The key word is 'undue,' not 'experimentation.'"" (citations omitted).

Applicants submit that a person of ordinary skill, equipped with the direction provided by the specification in combination with the skills possessed by such person, would require no more than routine experimentation to screen and select polypeptides that fall within the scope of the claims. Accordingly, the claimed genus is sufficiently described to satisfy the requirements of § 112, 1st paragraph. The added claim limitation is supported in the application and does not constitute new matter. *See, e.g.,* p. 24, lines 2-7 and p. 48, lines 18-36 of the '328 application.

Rejection of claims 33-37 under 35 U.S.C. § 112, 1st paragraph, written description.

The Examiner has rejected claims 33 to 37 as "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, has possession of the claimed invention." The Examiner states that "the claims are drawn to a genus of polypeptides that is defined only by sequence identity" but that the specification "merely discloses *one* amino acid sequence of human PRO842 with SEQ ID NO:2." The Examiner observes that no biological functions are specified in the claims. The Examiner also asserts that applicants "have a single polypeptide with a specific function that have (sic) not been correlated to any particular structural regions."

The Examiner also cites two cases; namely, *Vas-Cath v. Mahurkar*, 19 USPQ3s 1111 (Fed. Cir.) and *Fiddes v. Baird*, 30 USPQ2d 1481 (BPAI). The first case is cited for the proposition that the "specification does not 'clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." The second case is cited for the proposition that the disclosure of a single bovine sequence of "FGF" did not establish written description for "mammalian FGFs".

As the Examiner properly notes, the evaluation of written description is based on the claimed invention. In the present case, the claims define polypeptides defined by reference to a specific "human" polypeptide (SEQ. ID NO:2), that is fully described in the specification. The specification not only provides the structure of that polypeptide, but also provides information establishing certain functional characteristics of this polypeptide. The claims are not unlimited in their scope; nor do they attempt to claim polypeptide sequences whose relationship – in terms of structure and function – cannot be identified based on the disclosure provided. Instead, the claims are directed to a finite range of polypeptide structures that are defined by reference to a particular polypeptide sequence which the Examiner seems to acknowledge has been fully described by the present specification.

The claims do not attempt to define the invention by some unknown or unclear relationship of the claimed polypeptide sequences to the referenced polypeptide sequence (i.e., SEQ. ID NO:2). In this respect, *Fiddes v. Baird* is readily distinguishable from the present application. In *Fiddes*, the applicant claimed a range of sequences (i.e., all "mammalian FGF" sequences) the structure, function, or even existence of which could not be deduced from the

disclosure that was actually provided (i.e., a bovine FGF sequence). The present claims do not attempt to define the scope of the invention in prospective manner. Instead, the claims are directed to sequences that share a clearly defined structural similarity to a known and fully characterized polypeptide.

The Examiner has also made references to "portions" of the sequence that are or are not conserved. As the Examiner notes, the claims are the basis of the assessment of a written description analysis. In the present application, the applicant has not claimed polypeptides having particular *partial* sequences, the significance of which has or has not been established. Instead, the applicant has described an intact, complete polypeptide sequence having a particular biological significance and function, and presented claims to a range of structurally similar polypeptides using terms that are readily understood to a person skilled in the art (i.e., overall percent homology to a single sequence). The disclosure thus provides a description that a person skilled in the art can readily employ to identify the polypeptides that are encompassed by the claims.

Based on the foregoing, Applicants submit that the invention defined by the claims is fully described by the instant disclosure, and respectfully requests the Examiner to withdraw the rejection of claims 33 to 37 based 35 U.S.C. 112, first paragraph, written description.

Rejection of Claims 33-42 under 35 U.S.C. § 102(b) as being anticipated by Lal, *et al.*, WO 200000610-A2 ("Lal")

The Examiner asserts that *Lal et al.*, "discloses a polypeptide, a human signal peptide-containing protein having an amino acid sequence of SEQ ID NO:94, which is 100% identical to SEQ ID NO:2 of the instant invention." The Examiner also asserts that *Lal et al.*, teaches that SEQ ID NO:94 is a signal peptide-containing protein, indicating a mature protein lacking the signal peptide and therefore anticipates claim 40. Finally, the Examiner asserts that *Lal et al.*, teaches a fusion protein comprising said polypeptide and a heterologous moiety and therefore anticipates claim 42.

Applicant submits that this rejection is improper for several reasons, and respectfully requests the Examiner to withdraw this rejection.

As an initial matter, Applicant maintains that the current claims are entitled to a priority date of a least 8/24/00 as explained above. *Lal et al.,* was published on 1/6/00, less than one year prior to the Applicant's effective filing date. As such, Lal et al., is not prior art under § 102(b). On this basis, Applicant respectfully requests the Examiner to remove the § 102(b) rejection over Lal.

Applicant also notes that, under the legal standards used to evaluate whether a printed publication is sufficient to constitute a bar to patenting under 35 U.S.C. 102(b), *Lal et al.*, is insufficient to be prior art to the presently claimed invention. To qualify as prior art, a printed publication must enable those skilled in the art to "understand the nature and operation of the invention and carry it into practical use." See, *In re LeGrice*, 301 F.2d 929, 936, 133 U.S.P.Q. 365 (C.C.P.A. 1962) ("The public purpose of section 102(b) is clear enough, and has been enunciated or assumed in the very considerable body of decisional law in which the clause 'described in a printed publication' has been interpreted with respect to whether the publication has in fact conveyed such knowledge of an invention to the public as to put the public in possession of the invention."). If a printed publication fails to enable one skilled in the art to carry an invention into pratical use (e.g., because it fails to adequately describe or it fails to teach how to use the subject matter), it cannot be a bar to patenting under 35 U.S.C.§102(b).

The Examiner may consider Lal *et al.*, nonetheless, to constitute prior art to the current claims under 35 U.S.C. §102(e). In anticipation of such a conclusion, Applicant submits the following remarks.

It is well established that for a patent – and by implication, a published patent application – to be entitled to a priority date under 35 U.S.C. §120, it must enable one skilled in the art to make and use the claimed invention. *See, e.g., In re Wertheim and Mishkin*, 209 USPQ 554 (CCPA 1981); *Ex Parte D,* 27 USPQ2d 1067 (BPAI 1993). Consequently, for a patent or a published patent application to be accorded an effective prior art date under §102(e), including a date earlier than the actual filing date of the patent or published patent application, the application to which a claim of priority is made must also satisfy the requirements of 35 U.S.C. §112, first paragraph with respect to the subject matter at issue. Accordingly, for a rejection based upon this published patent application to be proper under 35 U.S.C §102(e), the publication must disclose enough information to enable a person skilled in the art to make and

use the invention, including information that establishes a specific, substantial and credible utility for the invention that is claimed in that application.

Under either the standards articulated for sufficiency of disclosure of a printed publication under 35 U.S.C. §102(b), or under those that govern patents and printed publications under 35 U.S.C. §102(e), the *Lal et al.* disclosure is insufficient to be prior art to the presently claimed invention. A careful review of *Lal et al.*, shows that this disclosure fails, in fact, to identify any specific or substantial utility for the polypeptide of SEQ ID NO:94. *Lal et al.,* discloses a total of 134 human signal peptide-containing proteins (referred to in *Lal et al.,* and hereinafter as "HSPP") and their corresponding nucleotide sequences, but provides nothing more than generic recitations regarding the use of those polypeptide sequences. For example, *Lal et al.,* contains the following statements – none of which are specific to the polypeptide of SEQ ID NO: 94, but instead are cited to apply to all 134 sequences that are disclosed in the application – regarding *possible grounds* to support utility of the disclosed polypeptides:

- ...the expression of HSPP is closely associated with proliferative, cancerous, inflamed, cardiovascular, nervous, reproductive, hematopoietic/immune, and development tissue. Therefore, HSPP appears to play a role in cell proliferation disorders including cancer; inflammation; and cardiovascular, neurological, reproductive, and developmental disorders. Page 40, lines 10-15.
- In the treatment of cell proliferative disorders...associated with increased HSPP expression or activity, it is desirable to decrease the expression or activity of HSPP. Page 4, lines 15-18.
- In the treatment of ...conditions associated with decreased HSPP expression or activity, it is desirable to increase the expression or activity of HSPP. Lal goes on to list approximately 300 diseases or conditions that may possibly be treated by increasing HSPP expression or activity. Page 40, line 18 – page 43, line 6.

Applicant submits that none of the above-disclosures is sufficient to provide a specific or substantial utility for the HSSP polypeptide encoded by SEQ ID NO:94. It appears that the purported utility for the disclosed HSSP polypeptides is grounded merely on a tissue distribution analysis and fails to provide any data that can reasonably establish any biological function of the HSPP of SEQ ID NO:94 that could provide a specific, substantial and credible utility.

Lal et al., also provides certain information regarding the HSSP of SEQ ID NO:94 (and the nucleotide sequence that encodes it (SEQ ID NO:228)) in Tables 1, 2, and 3, which is incorrect. For example, Lal predicts that the signal sequence of the polypeptide in Table 2 has a length of 22 amino acids. See page 100 of Lal. The actual length of the signal sequence, however, has been shown to be 26 amino acids. In Table 3, Lal provides a description of the tissue distribution patterns of the nucleic acid sequence that encodes the polypeptide of SEQ ID NO:94 as determined by northern blot analysis. Based on that expression pattern, *Lal et al.*, predict that expression of the polypeptide of SEQ ID NO:94 will be associated with certain diseases, disorders and conditions. Lal does not disclose, however, any comparisons between expression of this sequence in abnormal (e.g., tumor) tissue. For example, according to Table 3 in *Lal et al.*, the HSSP of SEQ ID NO:94 is expressed in cardiovascular, reproductive and urologic tissue. Solely on this basis, Lal et al., predict that expression of this sequence is implicated in cancer, inflammation and fetal or proliferating diseases or conditions. However, by failing to characterize expression of the sequence in abnormal versus normal tissue, these showings in *Lal et al.*, are meaningless. Simply put, a person of skill in the art would attach no significance to the expression data as presented because no comparisons are made between abnormal and normal tissue. Applicant notes that neither the information in Table 2 or 3 is sufficient to establish a specific or substantial utility for the polypeptide. The attempt by *Lal et al.*, to predict the utility of the polypeptide on incomplete and insufficient tissue distribution data fails to disclosure a specific, substantial or credible utility for the currently claimed polypeptide.

A disclosure that fails to set forth a specific, substantial or credible utility, by definition, means that the disclosure cannot teach a person of ordinary skill how to use the subject matter. See, *In re Brana*, 51 F3d 1560, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995). As set forth above, *Lal et al.*, does not satisfy the requirements of § 101 and cannot, therefore, constitute an anticipatory reference under § 102(b) or (e).

Rejection of Claims 33-38 and 40 under 35 U.S.C. § 102(b) as being anticipated by Rosen, *et al.*, WO 98/45712 ("Rosen")

The Examiner asserts that Rosen discloses a human polypeptide having an amino acid sequence of SEQ ID NO:53, which comprises residues 27-119 of SEQ ID NO:2 of the instant invention with 100% sequence identity. According to the Examiner, Rosen therefore anticipates claims 33-38 and 40 of the instant invention as a polypeptide of Figure 2 lacking its associated signal peptide.

Applicants have amended the claims to require that the polypeptides have at least 80% homology to the polypeptide of SEQ ID NO:2. Rosen does not disclose a polypeptide sequence having at least about 80% identity to the polypeptide of SEQ ID NO:2. Neither sequence disclosed in Rosen that shares some degree of homology to the polypeptide of SEQ ID NO:2 (i.e., SEQ ID NOS: 53 and 38) disclose a polypeptide have at least 80% identity to SEQ ID NO:2. For example, SEQ ID NO:53 of Rosen (relied on by the Examiner to reject claims 33-38 and 40) discloses a polypeptide that has only approximately 78% identity to the polypeptide of SEQ ID NO:2. SEQ 38 has approximately 50% identity to SEQ ID NO:2. Accordingly, Rosen does not disclose a polypeptide sequence that falls within the scope of the amended claims. As such, Rosen et al., does not anticipate the present claims.

Rejection of Claim 43 under 35 U.S.C. § 103(a) as being obvious over *Lal et al.*, in view of U.S. Patent No. 5,116,964 (Capon)

Claim 43 is rejected over *Lal et al.*, in view of *Capon et al.* The Examiner acknowledges that *Lal et al.*, does not teach a fusion protein of the claimed polypeptide. However, the Examiner asserts that *Capon et al.* disclose a novel polypeptide comprising an immunoglobulin Fc region and a target protein sequence for use, among other things, to extend the *in vivo* half-life of the resulting fusion protein. The Examiner further asserts that one of ordinary skill in the art would have been motivated to use the polypeptide disclosed in *Lal et al.*, to make a fusion protein as taught by Capon in order to, for example, facilitate protein purification.

For the reasons presented above, Applicant maintains that *Lal et al.*, is not prior art under 35 U.S.C. § 102(b) or (e) to the present claims. As such, Applicants believe a rejection under 35 U.S.C. 103(a) of claim 43 in view of Lal et al., alone or in view of any other reference, is inappropriate.

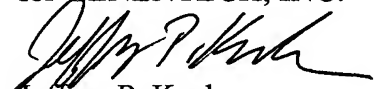
In addition, Applicants submit that the teachings of *Capon et al.*, fail to provide sufficient motivation or direction to modify the teachings of *Lal et al.*, to arrive at the subject matter of claim 43. The Capon et al., disclosure does not, for example, suggest that polypeptides of the class or having a structure comparable to that of SEQ ID NO:2 could or should be modified in the manner that is claimed.

For the above reasons, Applicant respectfully requests the Examiner to withdraw the rejection of claim 43 under § 103(a) based on *Lal et al.*, taken in view of *Capon et al.*.

Additional Comments

In view of this response, Applicant submits that the present application is in condition for allowance and should be passed to issue. If the Examiner believes that the application is not in condition for allowance or cannot be passed to issue in view of this response, Applicant respectfully requests that the Examiner contact the undersigned prior to taking any further action in this application.

Respectfully submitted,
for GENENTECH, INC.



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